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| 10/032,657 | 12/28/2001 | Sukanta Banerjee | B252 1280US | 6168 |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

**ADVISORY ACTION**

***Priority***

This application, 10032657, filed 12/28/2001 is a continuation in part of PCT/US01/20179, filed 06/21/2001 PCT/US01/20179 which claims priority from Provisional Application60213106, filed06/21/2000.

***After-Final Amendment Entry & Claims Status***

The amendment filed on March 05, 2010 has been acknowledged and entered.

Claims 18-22 are pending and being examined.

***Claimed Invention***

18. (previously presented) A method of multiplex analysis of analytes in a solution, comprising:

providing a plurality of magnetically polarizable microparticles of two or more types wherein different types bear an optically distinguishable signature, and the different types display different capture moieties on their surfaces capable of binding to different analytes;

suspending the microparticles in a first solution containing, or suspected to contain analytes of interest, under conditions permitting the capture of analytes by the capture moieties, and wherein an optical signal is generated following such capture;

using a magnetic field to assemble the microparticles in a planar array on a designated section of a substrate, where said magnetic field is generated by coils or

magnets and is uniformly distributed over the surface of the substrate, and wherein the spacing between particles within the array can be varied by varying the strength of the magnetic field without moving the coils or magnets; and

imaging the optically distinguishable signatures associated with the microparticles and the optical signals, and correlating the optical signals with microparticles having particular optically distinguishable signatures to determine which analytes are bound by which capture moieties.

## *Maintained Rejection(s)*

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 18-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al. (US 7,115,884 filed on October 6, 1997) in view of Wang (US 6,013,531) and further in view of Farber (US 5,602,042).

Walt teaches a method of multiplex analysis of analytes in a solution, comprising providing a population of microspheres having a plurality of different subpopulations, each subpopulation comprises microspheres having distinct optical response signature

(see col. 5, lines 5-30) or each microsphere is encoded with a fluorescent dye (see col. 11, lines 6-10) and has capture moieties coated thereon for binding to the target analyte (see tables II and III); the microspheres are assembled into an array and a sample is added to such array; illuminating the array; decoding the array by comparing the response of the entire sensor array to a known analyte or to a library of optical response signatures for its corresponding bead subpopulation type, where the optical response signature to various analytes has been previously measured and recorded. (see col. 5, lines 5-29). The beads and array images are recorded with a CCD frame transfer camera (see col. 17, lines 38-40).

However, Walt fails to teach using magnetic beads and applying a magnetic field at various strength to form an assembly of beads; Walt also fails to teach replacing the first solution with a second solution in claim 21.

Wang teaches fluorescent magnetic beads for use as markers in assay comprising a polymeric core coated evenly with a layer of polymer containing magnetically responsive metal oxide and a fluorescent dye or a combination of fluorescent dyes. (see col. 1, line 40-col. 2, line 9). Wang teaches using the magnetic particles in an assay by incubating the magnetic particles with a sample, magnetically separate them from the sample (first solution) and wash three times and resuspend in 30 ul of IBS (see example 35).

It would have been obvious to one of ordinary skills in the art to use fluorescent magnetic beads as those taught by Wang as particles in the method of Walt because the magnetic fluorescent particle in Walt can be used as a separation means and as a

label at the same time and thus avoid the use of a second label molecule. Regarding claim 21, it is well known to one of ordinary skills in the art that after magnetic separation, a wash step must be performed to ensure all the non-bound molecules from the sample which might interfere with the detection are removed and a step of resuspending the magnetic particles bound with analytes in a buffer (second solution) is also a must in order to carry out the detection step as taught by Wang. It would have been obvious to one of ordinary skills in the art to replace the first solution (sample) with a second solution such as a buffer (IBS) as taught by Wang in the method of Walt to disperse the particles in such solution as a preparation for the detection step.

However, Walt and Wang fail to teach applying a various strength magnetic field to the magnetic beads to form an assembly of beads.

Farber teaches collecting particles such as cells tagged with magnetic beads against a solid surface using a magnet element which generates magnetic field at various strength to control the spatial distribution of the cells collected against the surface. Other configurations for spatially varying the magnetic field can use a distributed array of magnet elements that can be selectively activated and deactivated. (see col. 3, lines 59-65). Farber teaches a uniform distributed magnetic field by using the array of magnet elements which can be selectively activated and deactivated and the magnets array is not movable.

It would have been obvious to one of ordinary skills in the art to immobilize magnetic particles to a substrate using a magnetic field according to the method taught by Farber to assemble the magnetic particles into an array for use in the combined

method of Walt and Wang so that analysis can be performed directly on a surface for large scale identification or separation.

***Response to Arguments***

Applicant's arguments filed December 8, 2010 have been fully considered but they are not persuasive.

Applicants argue that Farber does not teach the magnetic assembly step recited in claim 18 as now amended. Specifically, Farber does teach that the magnetic field is uniformly distributed over the substrate surface. Applicants argue that the magnetic particles being uniformly collected against the substrate is not equivalent to a uniform magnetic field distributed against the substrate because Farber teaches a magnetic is fixed at one point on the periphery of a rotating disc disposed vertically above the plate (substrate) and notes that this configuration "achieves a more uniform spatial distribution of particles collected against the plate". (see col. 4, lines 3-9). Farber states that this rotating disk is a means for “spatially varying the magnetic field” (see col. 4, lines 5-7). Thus, applicants submit that the office's conclusion that because Farber teaches that the particles are "uniformly" collected against the plate, the magnetic field must be uniformly distributed is in error.

This is not found persuasive because Farber teaches that the magnet (12) in figure 1 generates a strong magnetic field and disperses throughout the entire volume of the fluid sample (which is on the substrate or the container). (see col. 7, lines 30-34). Thus, if the strong magnetic field is dispersed throughout the entire volume of the fluid

sample on the substrate (plate), then the magnetic field must be uniformly distributed on the plate. Thus, The magnetic field strength is not varied.

Applicants further submit that Farber fails to teach that the spacing between particles may be varied by varying the strength of the magnetic field. Although Farber teaches varying the magnetic field strength, this variation of the magnetic field does not result in varying the spacing between the magnetic particles.

This is not found persuasive because the claim 18 recites that "wherein the spacing between particles within the array can be varied by varying the strength of the magnetic field without moving the coils or magnets". Thus, it is interpreted as that it only takes a variation of the magnetic field strength to vary the spacing between the magnetic particles.

Since Farber teaches varying the magnetic field strength, such varying must vary the spacing between the magnetic particles as well. Although Farber does not discuss such varying in the spacing between the magnetic particles, such varying in the spacing must happen since it is a result of varying the strength of the magnetic field.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Pensee T. Do/
Examiner, Art Unit 1641
/Jacob Cheu/
Primary Examiner, Art Unit 1641